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**Development and preliminary testing of a brief clinical tool to enable daily monitoring of chemotherapy toxicity: The Daily Chemotherapy Toxicity self-Assessment Questionnaire (DCTAQ)**

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**ABSTRACT**

Close monitoring of chemotherapy toxicity can be instrumental in ensuring prompt symptom management and quality care. Our aim was to develop a brief clinical tool to enable daily assessment of chemotherapy toxicity, and investigate/establish its content validity, feasibility/applicability, internal consistency and stability. Development of the Daily Chemotherapy Toxicity self-Assessment Questionnaire (DCTAQ) was based on an initial item pool created from two scoping reviews. Expert panel review (*n*=15) and cognitive debriefing with patients with cancer (*n*=7) was used to establish content validity. Feasibility/acceptability, applicability (self-report v. interview-like administration), internal consistency (KR-20) and test-retest reliability (at 1-hour intervals) of the DCTAQ were field-tested with 82 patients with breast or colorectal cancer receiving active chemotherapy at eight hospitals. Initial development/content validity stages enabled item revisions and re-wording that led to a final, 11-item DCTAQ version with 10 core symptom items plus one open-ended 'any other symptom' item. Feasibility and acceptability were demonstrated through absence of participant withdrawals, absence of missing data and no complaints about tool length. The DCTAQ was found to have modest internal consistency (KR-20=0.56), but very good test-retest reliability. The DCTAQ is a brief clinical tool that allows for rapid and accurate daily assessments of chemotherapy toxicity in clinical practice.

**Keywords:** *Patient-reported outcomes; Cancer; Chemotherapy toxicity; Daily Chemotherapy Toxicity self-Assessment Questionnaire (DCTAQ); Reliability; Validity*

**Running title:** *Development/testing of the DCTAQ*

## INTRODUCTION

Chemotherapy is a primary treatment modality for cancer. By exerting their pharmacological properties on cancerous cells, chemotherapy agents can suppress tumour growth or eliminate residual disease. However, the likelihood for normal body cells and tissues to be affected in the process is always present; thus, the impact of chemotherapy toxicity (expressed as one or more symptoms experienced by the patient) cannot be underestimated (Yamagishi, Morita, Miyashita, & Kimura, 2009). Chemotherapy toxicity often leads to distressing symptoms (e.g. nausea, breathlessness, fever) and potentially life-threatening conditions (e.g. neutropenia), associated with impaired quality of life, infections, poor treatment adherence, and increased mortality (McKenzie et al., 2011; Saevarsdottir, Fridriksdottir, & Gunnarsdottir, 2010; Yamagishi et al., 2009), as well as significant costs for the healthcare system (Brearley et al., 2011). Close symptom monitoring during active chemotherapy is therefore considered a cornerstone of multidisciplinary oncology practice in order to manage symptoms promptly, prevent exacerbation or relapse, and plan care accordingly (Basch et al., 2016; Cleeland, 2007; Cleeland et al., 2000).

Despite recent advances, including attempts to boost prediction of the risk for chemotherapy toxicity (Extermann et al., 2012; Hurria et al., 2011), chemotherapy-related symptoms are not always optimally assessed and managed in everyday clinical practice (Breivik et al., 2009; National Institute of Cancer, 2009). In addition, there is on-going debate about how best to generate data about chemotherapy-related toxicity to inform cancer clinicians. Typically, standard methods of collection of patient information involve the completion of paper-based forms by clinicians, using invalidated and/or retrospective accounts from patients. These strategies have been criticised as inefficient, subject to recall bias, and not representative of the patient experience (Ethan Basch et al., 2009; Coolbrandt et al., 2011; Fromme, Eilers, Mori, Hsieh, & Beer, 2004; Trotti, Colevas, Setser, & Basch, 2007).

In recent years, the use of patient-reported outcome (PRO) measures in routine cancer care practice has been advocated as a means to overcome the aforementioned limitations by facilitating a systematic approach that is based on the perspective of the patient (Flores et al., 2012; Gilbert, Sebag-Montefiore, Davidson, & Velikova, 2015; Howell et al., 2015). The use of PRO measures may result in the quicker reporting of symptoms through more frequent discussions with health professionals, improvement in the identification of bio-psychosocial problems that are often overlooked within routine practice, enhanced management of treatment toxicity, reduced hospitalisations, better adherence to chemotherapy, increased quality of life, and increased satisfaction with care (Basch et al., 2016; Donaldson, 2008; Kotronoulas et al., 2014; Snyder et al., 2012; Wu & Snyder, 2011). Several PRO measures and systems, including the Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) measurement system (Basch et al., 2014) and patient-reported adverse events (PRAE) system (Holch et al., 2016), have thus far been developed specifically to facilitate detection of chemotherapy toxicity (Armes et al., 2014; Brown et al., 2001; Kushner et al., 2008; Leonard et al., 2005; Postma et al., 2005; Sitzia, Dikken, & Hughes, 1997). However, they collectively present with critical limitations. These limitations include a focus on

individual symptoms (Kushner et al., 2008; Leonard et al., 2005; Postma et al., 2005) that fails to address the synergistic and cumulative nature of the symptom experience (Lenz, Pugh, Milligan, Gift, & Suppe, 1997; Miaskowski, 2004); lengthy measures that challenge implementation and use in busy clinical settings (Armes et al., 2014; Brown et al., 2001; Sitzia et al., 1997); incomplete information on the spectrum of the symptom experience (Sitzia et al., 1997); and lack of symptoms descriptors to assist patients to accurately report their symptoms (Brown et al., 2001; Sitzia et al., 1997). 'Generic' symptom assessment measures have also been used in this context (Bruera, Kuehn, Miller, Selmser, & Macmillan, 1991; Cleeland et al., 2000; de Haes et al., 1996; Portenoy et al., 1994). These measures have been developed for general use in cancer care, i.e. irrespective of type of cancer, treatment or phase; thus, whether they can accurately capture the specifics of chemotherapy toxicity assessment and grading may be questioned.

One key limitation of all available PRO measures for chemotherapy toxicity assessment is the use of prolonged time-frames for recall. With acute presentation and wide fluctuation in chemotherapy toxicity prevalence, severity and distress (Gilbert et al., 2015), even a 7-day recall window may be inadequate to provide accurate and relevant symptom information (Sitzia et al., 1997). In contrast, daily toxicity assessments can lead to a dramatic increase of the clinical relevance of symptom data (Gilbert et al., 2015). If facilitated through brief patient self-reports and focussed on a comprehensive evaluation (prevalence, severity, distress) of common chemotherapy symptoms, daily toxicity assessments can allow for well-informed clinical decision-making, prompt symptom management and over-time examination of symptom patterns to tailor patient care. The aim of this study was therefore to develop the Daily Chemotherapy Toxicity self-Assessment Questionnaire (DCTAQ) as a novel PRO measure to enable close monitoring of chemotherapy toxicity in clinical practice, and generate evidence to establish its content validity, feasibility/acceptability, internal consistency, and test-retest reliability (stability).

## METHODS

### Development of a pilot DCTAQ

The DCTAQ was developed as part of a larger research programme that evaluated clinical implementation of the Advanced Symptom Management System (ASyMS) (Kearney et al., 2009; Kearney, Maguire, Kotronoulas, & McCann, 2016) with patients with breast or colorectal cancer during adjuvant chemotherapy. We specifically targeted breast and colorectal cancers as two of the most prevalent types of cancer for which highly cytotoxic chemotherapy is administered, and therefore close toxicity monitoring is key. Scale items were generated from the two scoping literature reviews that aimed to identify the most prevalent toxicities experienced by patients receiving chemotherapy for breast or colorectal cancer. In the interest of clinical relevance, the ten most prevalent symptoms were selected for inclusion in a pilot DCTAQ. These included nausea (feeling sick), vomiting (being sick), diarrhoea, constipation, sore mouth and/or throat, paraesthesia, sore hands and/or feet, flu-like symptoms/infection, tiredness, and pain. The pilot DCTAQ aimed to collect patients' self-reports on

each symptom's prevalence, severity and associated distress. Formatting of items and response options was similar to two existing symptom assessment questionnaires (de Haes et al., 1996; Portenoy et al., 1994).

Initial development of the pilot DCTAQ was followed by a combined, collaborative approach to establish its content validity by involving health professionals and patients (Gravetter & Forzano, 2012; Staniszewska, Haywood, Brett, & Tutton, 2012). Ethical approval was obtained from the Fife and Forth Valley Research Ethics Committee.

**Expert Content Review**

A multi-disciplinary expert panel of cancer clinicians was convened to review the pilot DCTAQ (Gravetter & Forzano, 2012), by focussing on such aspects as content, appropriateness, response format, and wording of the pilot DCTAQ. The expert panel included nurses (*n*=9; including nurse practitioners, nurse consultants, and Macmillan nurse consultants) and allied health professionals (*n*=6; including pharmacists, team leaders, clinical service managers, and clinical learning facilitators), all with extensive experience in cancer care.

**Cognitive Debriefing Exercise with Patients**

Feedback from expert content review was incorporated into the pilot DCTAQ. The tool was then submitted to a cognitive debriefing exercise (Demuro, Lewis, Dibenedetti, Price, & Fehnel, 2012) with seven patients with breast or colorectal cancer, who were either receiving active-phase chemotherapy or had received chemotherapy in the past six months; this ensured diversity in patients' symptom experiences which was crucial for the pilot stage. Patients completed the pilot DCTAQ and reviewed its content, in order to establish readability, comprehension, relevance and appropriateness of DCTAQ items (Gravetter & Forzano, 2012). Open-ended, closed-ended and probing questions were used to elicit information. All comments were recorded on pro-forma sheets.

**Field Testing of the DCTAQ**

Patient feedback at the pilot stage was used to develop the final version of the DCTAQ. Field testing of the DCTAQ was carried out as part of the parent project. Patients involved in the pilot stage were not involved in the field testing stage. Patients eligible for participation in the field testing had a histologically confirmed diagnosis of breast or colorectal cancer; had a plan to receive ≥4 cycles of adjuvant chemotherapy as in-patients or outpatients; were 18 years old or older; were able to read/write/speak English; were physically and psychologically fit to participate in research as determined by a member of the healthcare team; and were able to provide written informed consent. Recruitment took place at eight clinical sites across the UK. Participants completed the DCTAQ twice (test/retest) during their first chemotherapy cycle, with a 1-hour time interval between the two

assessments. This time interval was considered appropriate to not only accommodate fluctuations in fast-changing symptoms, but also ensure that patients would not recall their initial responses.

### Data Analysis

Feasibility and acceptability analyses included calculation of missing values, DCTAQ-related withdrawals (*n*, %) and median time to complete the DCTAQ. Internal consistency of the DCTAQ was determined through calculation of item-to-item phi correlations and the Kuder-Richardson formula 20 (KR-20) for measures with dichotomous responses (yes/no on symptom prevalence) ((Kuder & Richardson, 1937). Test-retest reliability of DCTAQ dichotomous responses (yes/no on symptom prevalence) was assessed with % of absolute agreement that indicated the proportion of cases where symptom prevalence was reported the same on the test and retest DCTAQ. Cohen's kappa coefficients (κ value) were also calculated as they produce chance-corrected agreements (Dunn, 2009; Friedman & Wyatt, 2006). In addition, κ values were calculated separately by type of cancer, gender (colorectal cancer group only) and age (<55 v. ≥55 years based on a median-split approach) to further examine whether DCTAQ stability remained unaffected by these demographic variables. By convention, κ values of 0.60-0.80 indicated 'good' agreement, κ>0.80 denoted 'excellent' agreement, and κ=1 'perfect' agreement. Analyses were carried out in SPSS, v. 18 (IBM SPSS, Chicago, IL).

## RESULTS

### Content validity

The expert panel was involved in 2-6 consecutive review rounds. DCTAQ items were found to be understandable and relevant. Panel members positively commented on DCTAQ's brevity and comprehensiveness, as well as the use of a 24-hour recall period. Half of the panel members suggested that inclusion of descriptors/indicators of symptom severity would be beneficial to reduce patient confusion/misinterpretation and enhance accuracy of self-reports. If based on an existing taxonomy (e.g. the Common Terminology Criteria for Adverse Events [CTCAE] (National Institute of Cancer, 2009), symptom severity ratings could easily be translated into routine practice and incorporated into current management guidelines. Such descriptors (see Overview of the DCTAQ) were incorporated in the pilot DCTAQ, ahead of its distribution to patients during the cognitive debriefing exercise.

Overall, patients found pilot DCTAQ items to be understandable, relevant, and readable. A few items had to be reworded to enhance clarity. For instance, three patients indicated a lack of understanding of the term 'paraesthesia'. Whilst the word itself was unfamiliar, patients did understand the descriptors associated to this symptom. Nevertheless, the term 'paraesthesia' was replaced with the more descriptive term 'changes in sensation in your hands and/or feet'. Moreover, four patients noted that they had experienced symptoms not included in the pilot DCTAQ. They would welcome the option to report any additional symptoms to their clinical team. As a result, an eleventh item was included to

give the patient the option to report any additional symptoms. No further suggestions were made by the time seven patients had been recruited for the cognitive debriefing exercise, thus the pilot stage concluded with data collected from these seven participants.

### Overview of the DCTAQ

The DCTAQ is an 11-item, self-report measure that assesses 10 core chemotherapy-related symptoms. Item 11 invites the patient to report "any other symptoms". All items are set to be answered using a recall period of the past 24 hours. Three dimensions of chemotherapy toxicity are evaluated, namely symptom prevalence, symptom severity, and symptom distress. Symptom prevalence is reported on a dichotomous scale of yes/no for the eleven items. Where a 'yes' answer is received, the patient is asked to rate their symptom severity and symptom distress. A 3-point numerical scale (mild, moderate, severe) is used to evaluate symptom severity. The severity indicators have associated descriptors that are based on the CTCAE V4.0 taxonomy (National Institute of Cancer, 2009). Mild symptoms are defined using CTC 1 criteria, whilst CTC 2 criteria define moderate symptoms, and CTC 3 criteria define severe symptoms. Finally, a 4-point numerical scale (not at all, a little, quite a bit, very much) evaluates how much a patient is bothered/distressed by the symptom. The item relating to 'pain' also asks the patient to indicate the location of his/her pain on a body map, and whether the pain is new. Patients have the option to report up to 4 different areas of pain regardless of location of pain.

### Feasibility and acceptability

Eighty-two patients completed the DCTAQ during the field testing. The typical participant had an average age of 56 years (29-75). Most participants were diagnosed with breast cancer (59.6%; n=48). Seven out of ten patients with colorectal cancer were diagnosed with stage III disease; for patients with breast cancer, stage III disease accounted for 57% of the cases (**Table 1**). Regardless of cancer type, the most frequently reported symptoms were tiredness (*n*=48; 58.5%) and pain (*n*=24; 30%), followed by changes in sensation in hands and/or feet (*n*=21; 26%). Nausea, vomiting, diarrhoea and constipation were the symptoms least reported in this sample (*n*=0-4; 0-5%).

In terms of completeness of data, missing values on the DCTAQ were kept to a minimum, i.e. <1% of all available data. No patient commented on the length of the DCTAQ or withdrew. When asked whether DCTAQ items accurately captured the patient's symptom, >90% of participants confirmed this across all of the DCTAQ items. Completion of the DCTAQ required 10-12 minutes of the patient's time.

### Internal consistency

Internal consistency analyses revealed only modest reliability for the DCTAQ. A KR-20 coefficient of 0.56 was calculated. Item-to-item phi correlation coefficients ranged from -0.10 to 0.48.

**Test-retest reliability**

κ coefficients indicated a high level of agreement in the total sample, with items on diarrhoea, constipation, flu-like symptoms exhibiting perfect agreement (**Table 2**). For patients with breast cancer the lowest level of agreement was for items on 'feeling sick' and 'sore mouth and/or throat', with κ values just above 0.60. For patients with colorectal cancer, the lowest levels of agreement were for 'changes in sensation in hands and/or feet' (κ=0.76) and 'sore hands and/or feet' (κ=0.77).

Excellent-to-perfect agreement was found for most items based on male/female split (**Table 3**), except for 'sore hands and/or feet' (κ=0.63) in female participants, and 'changes in sensation in hands and/or feet' in male participants (κ=0.64). Excellent-to-perfect agreement was also found based on the age split. Excellent-to-perfect agreement was found in the '<55' age group for all items where sufficient information allowed calculation of κ values. Good agreement was found in the '≥55' age group for such items as 'sore mouth and/or throat' (κ=0.63 breast cancer group; κ=0.64 colorectal group), 'changes in sensation in hands and/or feet' (κ=0.68 colorectal cancer group) and 'sore hands and/or feet' (κ=0.60 colorectal cancer group).

## DISCUSSION

The DCTAQ is a new tool for use in clinical practice that was developed because of the clinical need for close monitoring of chemotherapy toxicity and in recognition of the limitations of current available questionnaires (see Introduction section). Indeed, the DCTAQ is a comprehensive clinical tool, specifically developed for use in chemotherapy settings, that employs patient self-reporting and a short (past 24 hours) time window to capture patients' experiences in relation to 10 core chemotherapy-related symptoms (plus any additional symptoms). Its brevity, short time-frame for recall, and embedded symptom descriptors make it appropriate for everyday use by patients receiving in-patient or outpatient chemotherapy to enable close and accurate symptom monitoring by the clinical team. As such, the DCTAQ can be seen as a means to mitigate current expressed concerns about the quality of chemotherapy toxicity assessments in clinical practice (Beijers, Mols, Van Den Hurk, & Vreugdenhil, 2016).

Our findings support the content validity, feasibility/acceptability and stability of the DCTAQ in assessing chemotherapy toxicity in this sample of patients with breast or colorectal cancer. Content validity was maximised by capturing the perspectives of both patients and clinicians, in line with current literature that considers patient and clinician involvement as a key component in the development process to enhance the quality, applicability and acceptability of a PRO measure (Staniszewska et al., 2012), and to "ensure that the product has a coherent fit with the care process" (p. 1143) (Richardson, Medina, Brown, & Sitzia, 2007). To that end, participation of patients and clinicians from multiple clinical sites/regions across the UK ensured that a necessary level of diversity in individual educational (patients) and/or clinical backgrounds (health professionals) was reached. The success of this approach was reflected on the questionnaire's documented feasibility/acceptability, given the absence of DCTAQ-related drop outs, the limited number of missing data and the reported high levels of item

accuracy based on patient feedback during subsequent field testing. It is possible that the inclusion of CTCAE toxicity descriptors corresponding to three levels of symptom severity (mild, moderate and severe) may have contributed to such favourable outcomes, owing perhaps to enhanced patient comprehension and interpretation of DCTAQ items. The wide subjectivity of the experience of cancer-related symptoms as well as the lack of integration between PRO-based grading and clinician-based grading are recognised barriers to PRO-driven clinical assessments (National Institute of Cancer, 2009; Paice, 2004) . We believe that DCTAQ addresses the clinical need for a unified assessment method to enhance patient-clinician communication when it comes to chemotherapy toxicity assessment.

As an indicator of internal consistency, the KR-20 was only modest (0.56), given that values closer to 1 indicate higher internal consistency (Kuder & Richardson, 1937). A number of factors may have contributed to this modest coefficient, including a small number of items on the DCTAQ, a relatively small sample size, low variability in participants' responses, or testing a body of content that was not unified (i.e. assessment of symptom prevalence, but with different bio-behavioural symptom triggers that could affect prevalence of individual symptoms). Further investigation is required to confidently establish internal consistency of the DCTAQ.

The DCTAQ, however, does appear to have very good test-retest reliability when administered at 1-hour intervals, with κ coefficients for the total sample and cancer type subgroups exceeding cut-offs for excellent agreement (>0.80) for most of its items, and irrespective of type of cancer, gender or age. Still, a number of items were found to have lower levels of agreement. It is perhaps not surprising that for patients with breast cancer lower levels of agreement were observed for items such as 'feeling sick' and 'sore mouth and/or throat' as these toxicities have a rapid trajectory and can change over a relatively short period of time. Items such as 'changes in sensation in hands and/or feet' and 'sore hands and feet' were associated with lower levels of agreement for patients with colorectal cancer. This again may be a reflection of the trajectory of cutaneous and sensory toxicities associated with many of the chemotherapy regimens administered to this patient group (Driessen, de Kleine-Bolt, Vingerhoets, Mols, & Vreugdenhil, 2012; Nagore, Insa, & Sanmartin, 2000).

Recently, Beijers et al. (2016) proposed clinical use of an index to quantify the "burden of treatment" and allow clinicians to make prompt decisions, e.g. about modifying the chemotherapy protocol. Their view was that burden of treatment is expressed as a composite score that takes into account the number and severity of chemotherapy toxicity as well as the number of days between chemotherapy cycles that patients experienced said toxicity. To this direction, Beijers et al. recognised the absence of a fit-for-purpose tool (Beijers et al., 2016). DCTAQ seems to address this gap, and further research is warranted to examine whether such index score might be a useful addition in clinical practice.

Finally, with the advent of digital solutions such as mobile phone technology or tablet personal computers (Bennett, Jensen, & Basch, 2012), development of electronic versions PRO measures (ePRO measures) are expected to promote 'real-time' symptom monitoring and allow greater flexibility

in symptom management in terms of remote monitoring and symptom alerting (Gilbert et al., 2015). Following development of the DCTAQ, our group carried on to create the e-DCTAQ, the electronic equivalent of the DCTAQ for use with mobile phones and smartphones (to be reported on a separate publication). Briefly, symptom monitoring via the e-DCTAQ was coupled with the development of risk algorithms and an alerting system that, whenever a symptom was reported as exceeding a pre-determined cut-point, generated and sent alerts to acute care clinicians for action (Maguire et al., 2017).

**Limitations**

Some limitations in this study warrant comment. Although data were gathered from multiple clinical sites, our sample consisted of patients with good use of English, whereas almost no patients were from ethnic minority backgrounds. Our relatively small sample size also limits statistical power of our tests and may have prevented diversity in the patients' symptom profiles during field testing of the DCTAQ. Relatedly, small sized sub-groups prevented us from testing differences in psychometric performance of the DCTAQ by type of chemotherapy regimen. This is clear indication for future investigation. With regard to content validity of the DCTAQ, during the initial development stages, medical oncologists were invited to review the pilot DCTAQ, but no responses were received. Despite this limitation, we believe that our rigorous investigation of the literature and involvement of cancer care experts in successive review rounds has led to a PRO measure, whose status seems to be in line with medical oncologists' views and priorities for symptom reporting in clinical practice. Since initial development of the DCTAQ, we have embarked on additional work involving the DCTAQ (Maguire et al., 2017) and consultation with oncologists from around the world, who have confirmed the content format of the DCTAQ. Moreover, psychometric properties of the DCTAQ were investigated with patients with breast or colorectal cancer; hence, our findings might not apply to groups of patients with other types of cancer. Our goal was to provide clinicians with a chemotherapy toxicity assessment tool, whose properties may be transferrable to other cancer patient populations. Nevertheless, future research will need to be inclusive of patient samples with different types of cancer receiving diverse chemotherapy regimens. Along these lines, formatting of items and scale responses was similar to that of two widely established symptom assessment questionnaires, the Memorial Symptom Assessment Scale (Portenoy et al., 1994) and the Rotterdam Symptom Checklist (de Haes et al., 1996); this might be seen as a point in favour of validity, but definitely cannot be used to draw conclusions on the construct validity of the DCTAQ that will need to be confirmed in the near future. Finally, due possibly to the formation of our convenience study sample, who as per the parent study's protocol were involved in the test/retest exercise during their first chemotherapy cycle to reduce unnecessary burden, reporting of some chemotherapy-related symptoms was rather infrequent. This finding may not reflect the symptom experience of all patients and throughout the treatment phase, and may have contributed to the low variability in responses received on the DCTAQ.

## CONCLUSIONS

In sum, we developed and tested a new clinical assessment tool for chemotherapy toxicity, whose goal is to allow timely identification of patients requiring comprehensive symptom management and care during chemotherapy. Our findings demonstrate that the DCTAQ is highly relevant, and it can be easily incorporated in clinical practice and used daily by patients treated with chemotherapy. The DCTAQ has strong content validity and stability, while its additional feature of severity descriptors to enhance interpretation and reporting accuracy can enhance patient-clinician communication in favour of prompt symptom management. Future research in the psychometric properties of the DCTAQ will require replicating its internal consistency and stability, as well as exploring its construct validity. This work will require larger and more diverse patient samples, involvement of patients with types of cancer other than breast or colorectal, and patients at different stages of chemotherapy and with diverse chemotherapy protocols.

## CONFLICTS OF INTEREST

The authors declare that there are no personal or financial conflicts of interest with regard to this work. The authors declare that they have full control of all primary data and that they agree to allow the journal to review their data if requested.

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## TABLES

**Table 1.** Characteristics of the study participants

| Characteristic | Total sample (*n*=82) | Colorectal cancer group (*n*=34) | Breast cancer group (*n*=48) |
|---|---|---|---|
| | Mean±SD (min-max) | Mean±SD (min-max) | Mean±SD (min-max) |
| Age (years) | 55.8±10.8 (29-75) | 59.9±9.5 (43-74) | 52.9±10.8 (29-75) |
| | **n (%)** | **n (%)** | **n (%)** |
| Gender | | | |
| Male | 18 (22.0) | 18 (52.9) | 0 (0) |
| Female | 64 (78.0) | 16 (47.1) | 48 (100) |
| Stage of disease (UICC/TNM) | | | |
| 0 | 1 (1.2) | 0 (0.0) | 1 (2.1) |
| I | 13 (15.9) | 2 (5.9) | 11 (22.9) |
| II | 20 (24.4) | 6 (17.6) | 14 (29.2) |
| III | 47 (57.3) | 25 (73.5) | 22 (45.8) |
| IV | 1 (1.2) | 1 (2.9) | 0 (0.0) |
| Chemotherapy Regimen | | | |
| Oxaliplatin/De-Gramont | | 16 (47.1) | |
| De-Gramont | | 2 (5.9) | |
| Capecitabine | | 5 (14.7) | |
| Oxaliplatin/Capecitabine | | 9 (26.4) | |
| Capecitabine/De-Gramont | | 2 (5.9) | |
| FEC | | | 33 (68.7) |
| FEC-T | | | 10 (20.8) |
| AC | | | 1 (2.1) |
| Docetaxel | | | 1 (2.1) |
| FEC-T-H | | | 2 (4.2) |
| Docetaxel/Cyclophosphamide | | | 1 (2.1) |

*Abbreviations:* FEC – Fluorouracil, Epirubicin, Cyclophosphamide; AC – Adriamycin, Cyclophosphamide; FEC-T – Fluorouracil, Epirubicin, Cyclophosphamide, Docetaxel; FEC-T-H – Fluorouracil, Epirubicin, Cyclophosphamide, Docetaxel, Trastuzumab; De-Gramont – Folinic Acid, Fluorouracil; SD – Standard deviation

**Table 2.** Agreement in terms of κ statistic between the same questions asked 1 hour apart for the total sample (n=82) and for breast cancer patients (n=48) and colorectal cancer patients (n=34)

| CTAQ Item | Total sample | | | | Breast Cancer | | | | Colorectal Cancer | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Symptom prevalence *n* (%) | | % Agreement | κ (SE) | Symptom prevalence *n* (%) | | % Agreement | κ (SE) | Symptom prevalence *n* (%) | | % Agreement | κ (SE) |
| | Time 1 | Time 2 | | | Time 1 | Time 2 | | | Time 1 | Time 2 | | |
| 1. Feeling sick | 4 (4.9) | 3 (3.7) | 98.8 | 0.85 (0.15) | 2 (4.2%) | 1 (2.1%) | 97.9 | 0.66 (0.33) | 2 (5.9%) | 2 (5.9%) | 100 | 1.00 (0.0) |
| 2. Being sick | 0 (0.0) | 0 (0.0) | 100 | NA | 0 (0%) | 0 (0%) | 100 | NA | 0 (0%) | 0 (0%) | 100 | NA |
| 3. Diarrhoea | 4 (4.9) | 4 (4.9) | 100 | 1.00 (0.0) | 1 (2.1%) | 1 (2.1%) | 100 | 1.00 (0.0) | 3 (8.8%) | 3 (8.8%) | 100 | 1.00 (0.0) |
| 4. Constipation | 2 (2.4) | 2 (2.4) | 100 | 1.00 (0.0) | 1 (2.1%) | 1 (2.1%) | 100 | 1.00 (0.0) | 1 (2.9%) | 1 (2.9%) | 100 | 1.00 (0.0) |
| 5. Sore mouth/throat | 8 (9.8) | 7 (8.5) | 96.3 | 0.78 (0.12) | 4 (8.3%) | 2 (4.2%) | 95.8 | 0.64 (0.23) | 4 (11.8%) | 5 (14.7%) | 97.1 | 0.87 (0.05) |
| 6. Changes in sensation in your hands and/or feet | 21 (25.6) | 19 (23.2) | 95.1 | 0.87 (0.06) | 5 (10.4%) | 5 (10.4) | 100 | 1.00 (0.0) | 16 (47.1%) | 14 (41.2%) | 88.2 | 0.76 (0.11) |
| 7. Sore hands and/or feet | 7 (8.5) | 7 (8.5) | 97.6 | 0.84 (0.11) | 2 (4.2%) | 2 (4.2%) | 100 | 1.00 (0.0) | 5 (14.7%) | 5 (14.7%) | 94.1 | 0.77 (0.16) |
| 8. Flu-like symptoms/infection | 6 (7.3) | 7 (8.5) | 100 | 1.00 (0.0) | 4 (8.3%) | 4 (8.3%) | 100 | 1.00 (0.0) | 2 (5.9%) | 2 (5.9%) | 100 | 1.00 (0.0) |
| 9. Tiredness | 48 (58.5) | 51 (62.2) | 96.3 | 0.92 (0.04) | 26 (54.2%) | 29 (60.4%) | 93.8 | 0.87 (0.07) | 22 (64.7%) | 22 (64.7%) | 100 | 1.00 (0.0) |
| 10. Pain | 24 (29.7)* | 23 (28.4)* | 96.3* | 0.91 (0.05) | 9 (18.8%) | 8 (16.7%) | 97.9 | 0.93 (0.07) | 15 (44.1%) | 15 (44.1%) | 93.9** | 0.89 (0.08) |

*Notes:* NA – questions all answered 'No' so κ could not be calculated.
*Abbreviations:* SE – Standard error
*n=81; **n=33

**Table 3.** Agreement in terms of κ statistic between the same questions asked 1 hour apart according to gender and age for patients with colorectal cancer, and according to age for patients with breast cancer.

| | Colorectal cancer | | | | Breast Cancer | |
|---|---|---|---|---|---|---|
| | Gender | | Age | | Age | |
| **CTAQ Item** | **Female (n=16)** | **Male (n=18)** | **<55 yrs (n=12)** | **55+ yrs (n=22)** | **<55 yrs (n=30)** | **55+ yrs (n=18)** |
| | **κ (SE)** | **κ (SE)** | **κ (SE)** | **κ (SE)** | **κ (SE)** | **κ (SE)** |
| 1. Feeling sick | 1.00 (0.33) | 1.00 (0.0) | 1.00 (0.0) | NA | 1.00 (0.33) | NA |
| 2. Being sick | NA | NA | NA | NA | NA | NA |
| 3. Diarrhoea | 1.00 (0.0) | 1.00 (0.0) | 1.00 (0.0) | 1.00 (0.0) | 1.00 (0.0) | NA |
| 4. Constipation | 1.00 (0.0) | NA | 1.00 (0.0) | NA | NA | NA |
| 5. Sore mouth/throat | 1.00 (0.0) | 0.77 (0.22) | 1.00 (0.0) | 0.64 (0.33) | 1.00 (0.0) | 0.63 (0.33) |
| 6. Changes in sensation in your hands and/or feet | 0.87 (0.13) | 0.64 (0.18) | 0.86 (0.14) | 0.68 (0.17) | 1.00 (0.0) | 1.00 (0.0) |
| 7. Sore hands and/or feet | 0.63 (0.33) | 0.82 (0.17) | 1.00 (0.0) | 0.60 (0.25) | 1.00 (0.0) | NA |
| 8. Flu-like symptoms/infection | 1.00 (0.0) | 1.00 (0.0) | 1.00 (0.0) | NA | 1.00 (0.0) | NA |
| 9. Tiredness | 1.00 (0.0) | 1.00 (0.0) | 1.00 (0.0) | 1.00 (0.0) | 0.86 (0.10) | 0.87 (0.13) |
| 10. Pain | 0.88 (0.12)* | 0.88 (0.17) | 0.85 (0.14) | 0.89 (0.10)** | 0.90 (0.10) | 1.00 (0.0) |

*Notes:* NA – questions all answered 'No' so κ could not be calculated.
*Abbreviations:* SE – Standard error
*n=15; **n=21